

Attorney Dkt. No. PU3610USw
S/N 09/889,471

REMARKS

The Examiner has reported that copies of the references listed in the applicant's Information Disclosure Statement were not provided when the IDS was submitted. The references in the IDS were cited in the International Search Report for the PCT application from which this applications claims priority and, applicant believes, should have been provided to the Examiner. Applicant submits additional copies of the missing publications herewith.

The Examiner has rejected claims 1, 2 and 71-90 under 35 U.S.C 103(a) as being unpatentable over Cadman (1998) in view of Tzen et al. (1990). The Examiner states that Cadman teaches "that retroviral therapeutic agents (RTAs) cause lipodistrophy when administered to HIV-infected patients" and "that many protease inhibitors (PIs) bind to two human proteins that regulate lipid metabolism." The Examiner also states that Tzen et al discloses "murine mesenchymal stem cells that undergo adipocyte differentiation in vitro" and therefore, according to the Examiner, it would be obvious to one of ordinary skill in the art to utilize the mesenchymal stem cells in an RTA screening assay to assess the affects of the RTA's on lipid metabolism.

Applicant respectfully traverses the rejection. The Cadman reference does not teach that RTA's cause lipodistrophy and, to the contrary, outlines the then widening debate over the cause. Several hypothesis are presented in the reference. Moreover, the Cadman reference does not disclose the binding of PIs to proteins related to lipid metabolism, but rather, reports that the enzyme to which PIs bind is "structurally similar to regions on two proteins that regulate the breakdown of lipids." The reference explains that, based on the observed structural similarities in the proteins, Australlian researchers hypothesized that the PIs could bind to and thereby inhibit the two lipid regulating proteins. Cadman presents mulitple hypothesis about the cause of lipodystrophy in HIV-infected patients, and points out that the origins of the disorder are unclear.

The Tzen abstract discloses the potential of murine mesynchymal stem cells to differentiate into a variety of different cell types, though they have a predilection to

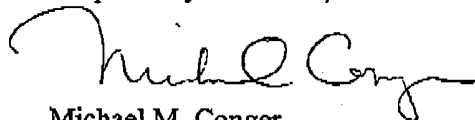
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undergo adipocyte differentiation. Tzen shows that EJras transfected cell lines lose their ability to differentiate to adipocytes. Nothing in the cited abstract suggests that the modulation of the differentiation pathway for the cell line shown in Tzen is related to inhibition of adipogenesis by an RTA. Combining the teachings of Tzen with the various hypothesis of Cadman does not render Applicant's invention obvious to one of ordinary skill in the art.

Applicants respectfully request the rejection be withdrawn.

Applicants believe that no fees are due in connection with the filing of this paper other than those specifically authorized herewith. However, should any other fees be deemed necessary to effect the timely filing of this paper the Commissioner is hereby authorized to charge such fees to Deposit Account No. 07-1392.

Respectfully submitted,



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